Bayer Diagnostics
ADVIA Centaur BNP Assay

APR 2 2 2005

Summary of Safety and Effectiveness

This Summary of Safety and Effectiveness has been prepared in accordance with the requirements of 21 CFR 807.92, to provide sufficient information to understand the basis for a determination of substantial equivalence.

1. Submitter Information

Contact Person: Carol Bianca

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Date Summary Prepared: October 18, 2004

2. Device Information

Propriety Name: ACS:180® and ADVIA Centaur® B-Type Natriuretic Peptide (BNP) Assays

Common Name: BNP assays

Classification Name: B-type natriuretic peptide test systems
Class: II
CFR: 21 CFR 862.1117
Product Code: NBC

3. Predicate Device Information

Name: ADVIA Centaur® B-Type Natriuretic Peptide (BNP) Assay

Manufacturer: Bayer Healthcare - Diagnostics Division
511 Benedict Ave.
Tarrytown, N.Y. 10591

510(k) Numbers: K031038; K040425

4. Device Description

The ACS:180 and ADVIA Centaur BNP assays are fully automated two-site sandwich immunoassays using direct chemiluminescent technology, which use constant amounts of two monoclonal antibodies. The first antibody, in the Lite Reagent, is an acridinium ester labeled monoclonal mouse anti-human BNP F(ab')2 fragment specific to the ring structure of BNP. The second antibody, in the Solid Phase, is a biotinylated monoclonal mouse anti-human antibody specific to the C-terminal portion of BNP, which is coupled to streptavidin magnetic particles. Patient sample (calibrator or control materials) is incubated for 5 minutes at 37°C with the Lite Reagent that contains the tracer antibody conjugate. Subsequently, Solid Phase reagent is added and incubated for 2.5 minutes at 37°C. An immuno-complex is formed between the BNP in the sample and the two antibody conjugates. Following incubation, the unbound antibody conjugates are washed away. The chemiluminescence of the immuno-complex signal is measured in a luminometer. Samples with low BNP levels will have a minimum amount of bound AE label, while samples with high levels of BNP will have maximum label complex bound. Thus, a direct relationship exists between the amount of BNP present in the patient sample and the amount of relative light units (RLUs) detected by the system.

5. Statement of Intended Use

ACS:180 BNP Assay

For *in vitro* diagnostic use in the quantitative determination of B-type Natriuretic Peptide (BNP) in human plasma using the ACS:180® Automated Chemiluminescence System. This assay is indicated for the measurement of plasma BNP as an aid in the diagnosis and assessment of the severity of heart failure. In patients with acute coronary syndromes (ACS), this test, in conjunction with other known risk factors, can also be used to predict survival as well as to predict the likelihood of future heart failure. This assay is not intended for use on any other system.

ADVIA Centaur BNP Assay

For *in vitro* diagnostic use in the quantitative determination of B-type Natriuretic Peptide (BNP) in human plasma using the ADVIA Centaur® System. This assay is indicated for the measurement of plasma BNP as an aid in the diagnosis and assessment of the severity of heart failure. In patients with acute coronary syndromes (ACS), this test, in conjunction with other known risk factors, can also be used to predict survival as well as to predict the likelihood of future heart failure. This assay is not intended for use on any other system.

6. Substantial Equivalence

The Bayer B-type Natriuretic Peptide (BNP) assays on the ACS:180® and ADVIA Centaur® are substantially equivalent to ADVIA Centaur® BNP assay. The ADVIA Centaur BNP Assay was cleared under K031038 on June 23, 2003, as an aid in diagnosis of heart failure. The ACS:180® BNP version has followed the new Replacement Reagent Policy guidance to allow its marketing under the same intended use. The ADVIA Centaur and ACS:180 BNP assays were cleared under K040425 on June 14, 2004, for the assessment of severity of heart failure and for use, in conjunction with other known risk factors, to predict survival in patients after myocardial infarction.

(a) Technological Characteristics

The following table compares the technology features of the current and proposed Bayer ADVIA Centaur and ACS:180 BNP assays:

Feature	Current Bayer ADVIA Centaur® and ACS:180® BNP Immunoassays	Proposed Bayer ADVIA Centaur® and ACS:180® BNP Immunoassays
Intended Use	Quantitative determination of B-type Natriuretic Peptide	Same
Indication for Use	An aid in the diagnosis and assessment of the severity of heart failure. Can also be used, in conjunction with other known risk factors, to predict survival in patients after myocardial infarction.	An aid in the diagnosis and assessment of the severity of heart failure. Can also be used, in conjunction with other known risk factors, to predict survival as well as to predict the likelihood of future heart failure in patients with acute coronary syndromes.
Assay Principle	Chemiluminescence immunoassay	Same
Traceability/Standardization	Reference standard – synthetic human BNP (amino acid 77 to 108) in buffer based matrix.	Same
Calibration Interval	• After 28 days (ADVIA Centaur), or 42 days (ACS:180), when using the same reagent lot • With every new primary reagent lot	Same
Sample Type	Human plasma using EDTA as anticoagulant	Same
Sample Volume	100 µL	Same
Calibrator	BNP Calibrator set (2 levels)	Same
Controls	BNP 1,2,3 Quality Control set	Same
Reagent Stability	• Until the expiration date when stored at 2-8°C Onboard • ADVIA Centaur: 41.6 days (or 60 days with the use of version 3.0 software or higher) • ACS:180: 72 hours	Same
Instruments	• ADVIA Centaur and ACS:180 Systems, fully automated, random-access immunoassay analyzers	Same
Measuring Range	• ADVIA Centaur: <2.0 – 5000 pg/mL • ACS:180: <15 – 5000 pg/mL	Same

(b) Performance Characteristics

The following table compares the performance characteristics of the current and proposed Bayer ADVIA Centaur and ACS:180 BNP assays:

Feature	Current Bayer ADVIA Centaur® and ACS:180® BNP Immunoassays	Proposed Bayer ADVIA Centaur® and ACS:180® BNP Immunoassays
Expected Values	• Age and gender-matched descriptive statistics provided • Decision threshold of 100 pg/mL recommended for diagnosis of heart failure. • Decision threshold of 80 pg/mL recommended for prediction of survival after myocardial infarction.	• Age and gender-matched descriptive statistics provided. • Decision threshold of 100 pg/mL recommended for diagnosis of heart failure. • Decision threshold of 80 pg/mL recommended for prediction of survival and future heart failure in patients with acute coronary syndromes.
Precision	ADVIA Centaur: • Within-run 1.8 – 4.3 %CV from 29.4 – 1736 pg/mL • Total 2.3 – 4.7 %CV from 29.4 – 1736 pg/mL ACS:180: • Within-run 2.5 – 7.9%CV from 51.5 – 1783 pg/mL • Total 3.8 – 9.9%CV from 51.5 – 1783 pg/mL	Same
Hook Effect	No high dose effect up to 100,000 pg/mL	Same
Analytical Sensitivity	• ADVIA Centaur: <2 pg/mL • ACS:180: <15 pg/mL	Same
Dilution Recovery	On-board dilution 1:2, 1:5 and 1:10 with average recovery of 97% on ADVIA Centaur and 98% on ACS:180.	Same
Limitations/Warning/ Precautions	• This test has been evaluated with plasma using EDTA as the anticoagulant. Serum, sodium citrate, lithium heparin and sodium fluoride sample tubes have also been tested and are not recommended. • No interference from hemoglobin up to 1000 mg/dL • No interference from triglycerides up to 800 mg/dL • No interference from cholesterol up to 1000 mg/dL • No interference from urea up to 200 mg/dL • No interference from	Same

Feature	Current Bayer ADVIA Centaur® and ACS:180® BNP Immunoassays	Proposed Bayer ADVIA Centaur® and ACS:180® BNP Immunoassays
	creatinine up to 2.5 mg/dL • No interference from unconjugated bilirubin up to 25 mg/dL • No interference from conjugated bilirubin up to 25 mg/dL • No interference from human IgG up to 5.3 g/dL • No interference from 55 commonly used pharmaceutical drugs. • Results should always be assessed in conjunction with the patient's medical history, clinical evaluation and other diagnostic procedures.	

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

APR 2 2 2005

Ms. Carol Bianca
Manager, Regulatory Affairs
Bayer HealthCare, LLC.
Diagnostics Division
511 Benedict Ave
Tarrytown, NY 10591

Re: k043228
Trade/Device Name: Bayer Diagnostics ADVIA Centaur® BNP Assay
Regulation Number: 21 CFR 862.1117
Regulation Name: B-type natriuretic peptide test system
Regulatory Class: Class II
Product Code: NBC
Dated: April 8, 2005
Received: April 12, 2005

Dear Ms. Bianca:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (240)276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html

Sincerely yours,

Jean M. Cooper MS, DVM

Jean M. Cooper, MS, D.V.M.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K043228

Device Name: Bayer Diagnostics ADVIA Centaur® BNP Assay

Indications For Use:

For *in vitro* diagnostic use in the quantitative determination of B-type Natriuretic Peptide (BNP) in human plasma using the ADVIA Centaur® System. This assay is indicated for the measurement of plasma BNP as an aid in the diagnosis and assessment of the severity of heart failure. In patients with acute coronary syndromes (ACS), this test, in conjunction with other known risk factors, can also be used to predict survival as well as to predict the likelihood of future heart failure. This assay is not intended for use on any other system.

Prescription Use ____X__ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Carol C. Benson
Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K043228

Indications for Use

510(k) Number (if known): K043228

Device Name: Bayer Diagnostics ACS:180® BNP Assay

Indications For Use:

For *in vitro* diagnostic use in the quantitative determination of B-type Natriuretic Peptide (BNP) in human plasma using the ACS:180® Automated Chemiluminescence System. This assay is indicated for the measurement of plasma BNP as an aid in the diagnosis and assessment of the severity of heart failure. In patients with acute coronary syndromes (ACS), this test, in conjunction with other known risk factors, can also be used to predict survival as well as to predict the likelihood of future heart failure. This assay is not intended for use on any other system.

Prescription Use ____X__ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

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Office of In Vitro Diagnostic
Device Evaluation and Safety

K043228